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**Filing Date:** 11 August 1998

IN THE CLAIMS:

Please enter the following amended claim set:

--59. (Amended) A method of subjecting a sample to rapid thermal cycling, said method comprising:

a) contacting a sample holder containing a sample with heated fluid, thereby raising the temperature of the sample to a first temperature, and holding the sample at about said first temperature for a first predetermined period of time;

b) contacting the sample holder with non-heated fluid, thereby lowering the temperature of the sample to a second temperature, and holding the sample at about said second temperature for a second predetermined period of time;

c) contacting the sample holder with heated fluid, thereby raising the temperature of the sample to a third temperature, and holding the sample at about said third temperature for a third predetermined period of time;

wherein steps a) through c) are completed in about 30-60 seconds; and

wherein said sample holder has a thermal mass which provides for completing said cycle in 30-60 seconds.

60. The method of Claim 59, wherein steps a) through c) are repeated.

61. The method of Claim 59 or 60, wherein said sample holder is one of a plurality of sample holders.

62. The method of Claim 59 or 60, wherein the first predetermined period of time is about 8 seconds or less.

63. The method of Claim 62, wherein the first predetermined period of time is less than 1

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second.

64. The method of Claim 59 or 60, wherein said lowering in step b) occurs in about 25 seconds or less.

65. The method of Claim 59 or 60, wherein said lowering in step b) occurs at an average rate of between at least about 1.5 °C per second and up to about 4.1 °C per second.

67. The method of Claim 59 or 60, wherein the difference between said first and said second temperature is up to about 42 °C.

68. The method of Claim 59 or 60, wherein the second predetermined period of time is about 5 seconds or less.

69. The method of Claim 68, wherein the second predetermined period of time is less than 1 second.

70. (Amended) A method of amplifying a nucleic acid, said method comprising:

a) heating a sample holder containing a sample comprising a nucleic acid and amplification primer, thereby raising the temperature of the sample to a first temperature, and holding the sample at about said first temperature for a first predetermined period of time to denature said double-stranded nucleic acid;

b) cooling the sample holder, thereby lowering the temperature of the nucleic acid sample to a second temperature, and holding the sample at about said second temperature for a second predetermined period of time to anneal said amplification primer;

c) heating the sample holder, thereby raising the temperature of the nucleic acid sample to a third temperature, and holding the sample at about said third temperature for a third predetermined period of time to allow amplification of said nucleic acid;

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d) repeating steps a) through c), wherein steps a) through c) are completed in about 30-60 seconds;

wherein said sample holder has a thermal mass which provides for completing said cycle in 30-60 seconds.

71. The method of Claim 70, wherein said sample further comprises a nucleic acid polymerizing enzyme.

72. The method of Claim 70, wherein said sample holder is one of a plurality of sample holders.

73. The method of Claim 70, wherein the first predetermined period of time is less than 1 second.

74. The method of Claim 70, wherein said lowering in step b) occurs in about 25 seconds or less.

75. The method of Claim 74, wherein said lowering in step b) occurs in about 9 seconds.

76. The method of Claim 70, wherein said lowering in step b) occurs at an average rate of between at least about 1.5 °C per second and up to about 4.1 °C per second.

78. The method of Claim 70, wherein the difference between said first and said second temperature is up to about 42 °C.

79. The method of Claim 70, wherein the second predetermined period of time is about 5 seconds or less.

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80. The method of Claim 79, wherein the second predetermined period of time is less than 1 second.

81. A method of subjecting a sample to rapid thermal cycling to amplify a nucleic acid, said method comprising:

a) raising the temperature of a sample to a first temperature and holding the sample at about said first temperature for a first predetermined period of time;

b) lowering the temperature of the sample to a second temperature at a rate at least about 1.5 °C per second and holding the sample at about said second temperature for a second predetermined period of time.

82. The method of Claim 81, further comprising:

c) raising the temperature of the sample to a third temperature intermediate to said first and second temperatures and holding the sample at about said third temperature for a third predetermined period of time.

83. The method of Claim 81 or 82, wherein the steps are repeated.

84. The method of Claim 81 or 82, wherein said lowering in step b) is at a rate of up to about 4.1 °C per second.

85. The method of Claim 81 or 82, wherein the difference between said first and said second temperature is up to about 42 °C.

86. The method of Claim 81 or 82, wherein the first predetermined period of time is about 8 seconds or less.

87. The method of Claim 81 or 82, wherein the first predetermined period of time is less

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than 1 second.

88. The method of Claim 81 or 82, wherein the second predetermined period of time is about 20 seconds or less.

89. The method of Claim 81 or 82, wherein the second predetermined period of time is less than 1 second.--.

90. The method of Claim 70, further comprising the step:  
e) detecting the amplification products by fluorescence.

#### **REMARKS**

Claims 59-65, 67-76 and 78-90 are pending in the instant application. Claims 66 and 77 are canceled, with their limitations combined into amended Claims 65 and 76. Claim 90 is new. Reconsideration of the claims in light of the remarks that follow is kindly requested.

Claim 59 has been amended to more clearly claim a sample holder that has a thermal mass that allows for the requisite heating and cooling cycle to be completed within 30-60 seconds. Support for this amendment can be found at page 23 lines 15-21 of the present specification and page 16 lines 1-7 of the '029 application.

Claim 62, depending from Claim 59 or 60, specifies that the first predetermined period of time is about 8 seconds or less. The first predetermined period of time refers to the denaturation period in Figure 6 of the present specification and U.S. Application Serial No. 07/534,029 (the '029 application). As is shown in Figure 6, by increasing the denaturation time to more than about 8 seconds, the product yield either remains static or, at even longer periods, eventually decreases. Conversely, by limiting the denaturation period to less than about 8 seconds the product yield increases.